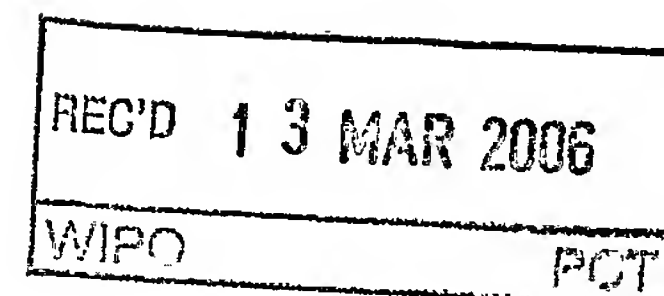


PATENT COOPERATION TREATY

PCT



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 5574-1001	FOR FURTHER ACTION		See Form PCT/IPEA/416																								
International application No. PCT/US05/05616	International filing date (<i>day/month/year</i>) 23 February 2005 (23.02.2005)	Priority date (<i>day/month/year</i>) 23 February 2004 (23.02.2004)																									
International Patent Classification (IPC) or national classification and IPC IPC(7): C12M 1/36 and US Cl.: 435/286.5, 287.3, 293.1, 304.2																											
Applicant DE CRECY, EUDES FRANCOIS MARIE																											
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p style="margin-left: 20px;">a. <input checked="" type="checkbox"/> (<i>sent to the applicant and to the International Bureau</i>) a total of <u>2</u> sheets, as follows:</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p style="margin-left: 20px;">b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																											
<p>4. This report contains indications relating to the following items:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 20%;">Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>				<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand 07 October 2005 (07.10.2005)		Date of completion of this report 28 February 2006 (28.02.2006)																									
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer Richard Crispino Telephone No. 571-272-1700 <div style="text-align: right;"> DEBORAH A. THOMAS PARALEGAL SPECIALIST <i>DA</i> </div>																									

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/US05/05616

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

- ☐ the international application in the language in which it was filed.
- ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4(a))
- ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

- ☐ the international application as originally filed/furnished
- ☒ the description:
 pages 1-9 as originally filed/furnished
 pages* NONE received by this Authority on _____
 pages* NONE received by this Authority on _____
- ☒ the claims:
 pages None as originally filed/furnished
 pages* NONE as amended (together with any statement) under Article 19
 pages* 10-17 received by this Authority on 07 october 2005
 pages* NONE received by this Authority on _____
- ☒ the drawings:
 pages 1-7 as originally filed/furnished
 pages* NONE received by this Authority on _____
 pages* NONE received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to the sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US05/05616

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-36</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-36</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-36</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and Explanations (Rule 70.7)

Claims 1-36 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the device of claim 1 and the method of using the device as described in claim 13, specifically a means for moving the clamps and tubing as defined.

1. A device that increases the rate of reproduction (through increased speed of reproduction and/or increased reproductive yield) of living cells in suspension or of any culturable organisms through the process of natural selection, said device comprising: a) a flexible, sterile tube containing culture medium,

b) a system of clamps, each capable of open and closed positions, the clamps being positioned so as to be able to divide the tube into separate regions containing spent culture (downstream region), growing culture (growth chamber), and fresh growth medium (upstream region),

c) a means of moving the clamps and the tubing such that a portion of the growth chamber and the associated culture can be clamped off and separated from the growth chamber, and such that a portion of fresh tubing containing unused medium can be joined with a portion of the culture and associated medium already present in the growth chamber, wherein each of the clamps does not move with respect to the tube when said clamp is in the closed position.

2. The device according to claim 1, wherein the tubing is flexible to allow clamping and segregation into separated chambers.

3. The device according to claim 1, wherein the tubing is gas permeable, for example comprised primarily of silicon, to allow gas exchange between the cultured organism and the outside environment, according to the type of experiment.

4. The device according to claim 1, wherein the tubing is gas impermeable, to prevent gas exchange between the tubing and the outside environment, if the experiment demands anaerobiosis.

5. The device according to claim 1, wherein the tubing is transparent or translucent, to allow the measurement of turbidity.

6. The device according to claim 1, wherein the growth chamber tubing and associated media and culture can be depressurized or over pressurized relative to ambient atmosphere as necessitated by experimental requirements.

7. The device according to claim 1, wherein the tubing allows the measure of pH of medium by inclusion of a pH indicator in the tubing composition or lining.

8. The device according to claim 1, wherein the growth chamber tubing and associated media and culture can be heated or cooled as appropriate for experiment conditions.

9. The device according to claim 1, wherein the growth chamber tubing and associated media and culture can be kept motionless or agitated by any already known method.

10. The device according to claim 9 wherein the tubing can include one or several stirring bars for agitation purpose.

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Patented 1965 by IPEA/US

11. The device according to claim 1 wherein regions of the tubing can be confined in a specific and controlled atmospheric area to control gas exchange dynamics.

12. The device according to claim 1 wherein the growth chamber tubing and associated media and culture can be tilted either downward to remove aggregated cells, or upward to remove air through the functions described in claim 1-c.

13. A method that increases the rate of reproduction (through increased speed of reproduction and/or increased reproductive yield) of living cells in suspension or of any culturable organisms through the process of natural selection, comprising: a) providing an initial culture in the described growth chamber through sterile injection of a starter culture into a sterile tube containing sterile growth medium; b) maintaining growth conditions according to experimental requisites ; c) after a certain period of time and associated growth of the culture, adjusting the position of the described gates so as to move equal portions of fresh medium and of grown culture (respectively) into and out of the region defined as the growth chamber, allowing the remaining portion of grown culture to mix with the introduced portion of fresh medium and continue to grow; d) reproducing steps b) and c) until the end of experiment to achieve continuous culture and selection of variants with increased reproductive rates; e) withdrawing on demand a sample of grown culture from sampling chamber.

15. A method according to claim 13 wherein an experiment can include as many growth cycles as required by the experimenter without possible contamination of isolated growing chamber and without possible proliferation of a dilution-resistant population.

17. A method according to claim 13 wherein a combination of tilting the device and operating agitators leads to an appropriate agitation for mixing the growing culture in order to prevent or repress aggregation of living organisms.

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a continuous length of flexible, sterile tubing;
a system of clamps positioned at points along a section of the tubing, each of the clamps being positioned and arranged so as to be able to controllably pinch the tubing by putting said clamp into a closed position in which the tubing is divided into separate regions on respective sides of said clamp, the separate regions on respective sides of said clamp being merged back into a single region when said clamp is returned to an open position;
wherein the clamps and tubing are arranged so that the tubing is clamped at first through fourth points along the tubing, defining first through third regions downstream of the first through third points, respectively; and
wherein a volume of the second region delimited by said points two and three is greater than a volume of the first and third regions.
wherein the system of clamps is constructed so that, in a repeating pattern, the tubing is clamped upstream of the first point, the tubing is clamped at a point between the second and third points, and the second point is returned to the open position, thereby subdividing the second region into an upstream portion and a downstream portion, merging the first region and the upstream portion, and thereby defining new first through fourth points and first through third regions.

19. The device according to claim 18, wherein the tubing is gas permeable.

20. The device according to claim 18, wherein the tubing is gas impermeable.

21. The device according to claim 18, wherein the tubing is translucent.

22. The device according to claim 18, wherein the tubing is transparent.

23. The device according to claim 18, wherein contents of the tubing in the second region can be controllably depressurized or over pressurized relative to ambient atmosphere.

24. The device according to claim 18, further comprising a pH indicator in the tubing.

25. The device according to claim 18, further comprising a heating and cooling device that can control a temperature of contents of the tubing.

26. The device according to claim 18, further comprising an agitator.

27. The device according to claim 26, wherein the agitator comprises at least one stirring bar.

28. The device according to claim 18, wherein regions of the tubing can be confined in a specific and controlled atmospheric area to control gas exchange dynamics.

29. The device according to claim 18, further comprising a device to control tilting of the second portion of the tubing.

30. A method that increases the rate of reproduction (through increased speed of reproduction and/or increased reproductive yield) of living cells in suspension or of any culturable organisms through the process of natural selection, said device comprising steps of:

providing a continuous length of flexible, sterile tubing;

providing a system of clamps positioned at points along a section of the tubing, each of the clamps being positioned and arranged so as to be able to controllably pinch the tubing by putting said clamp into a closed position in which the tubing is divided into separate regions on respective sides of said clamp, the separate regions on respective sides of said clamp being merged back into a single region when said clamp is returned to an open position;

placing culture medium in the tubing;

closing the clamps at first through fourth points along the tubing to define first through third regions downstream of the first through third points, respectively, wherein the volume of the second region delimited by said points two and three is greater than a volume of the first and third regions;

introducing said culturable organism into the second region between the second and third points, and allowing the culture to grow in the culture medium; and

repeating a step that comprises clamping the tubing upstream of the first point, clamping the tubing at a point between the second and third points, and returning the second point to the open position, thereby subdividing the second region into an upstream portion and a downstream portion, merging the first region and the upstream portion, and thereby defining new first through fourth points and first through third regions.

31. The method of claim 30, wherein applying a simultaneous peristaltic movement of the clamps, the tubing, and the medium and the culture within the tubing, allows provision of a certain quantity of fresh said medium to the second region of the tubing while an equal quantity of said culture is isolated and removed through an opposite end of said second region, terminating one growth cycle and starting a new growth cycle.

32. The method of claim 30, further comprising a step of controlling a pressure of contents of the tubing in the second region.

33. The method of claim 30, further comprising a step of controlling a temperature of contents of the tubing.

34. The method of claim 30, further comprising a step of agitating contents of the tubing.

35. The method of claim 30, further comprising a step of providing a specific and controlled atmospheric area around the tubing to control gas exchange dynamics.

36. The method of claim 30, further comprising a step of controllably tilting of the second portion of the tubing.